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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/421,778	10/19/1999	JAMES T. FULLER	APF-30.20	4604

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/421,778	FULLER, JAMES T.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11-16,20-23,25,28,29,31-33,35,36 and 38-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11-16,20-23,25,28,29,31-33,35,36 and 38-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 10/14/05 has been entered even though it does not technically comply with 37 CFR 1.121(c) because existing periods were underlined in amended claims 1, 15, 21 and 25. For the purpose of a compact prosecution, the Examiner agreed to enter the Amendment (also see Interview Summary).

Accordingly, amended claims 1-7, 11-16, 20-23, 25, 28-29, 31-33, 35-36, 38-41 are pending in the present application and they are examined on the merits herein.

Response to Amendment

The rejection of claim 38 under 35 U.S.C. 112, first paragraph, was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(b) as being anticipated by Hofmann et al. (Proc. Natl. Acad. Sci. 93:5185-5190, 1996) was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(e) as being anticipated by Chao (U.S. Patent No. 6,368,825) was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(e) as being anticipated by Johnston et al. (U.S. Patent No. 6,194,389; IDS, AK-1) was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(b) as being anticipated by Lai et al. (DNA Cell Biol. 14:643-651, 1995; Cited previously) was withdrawn in light of Applicant's amendment.

. The rejection under 35 U.S.C. 102(b) as being anticipated by Haynes et al. (AIDS Res. Hum. Ret. 10, Supplement 2, pages S43-S45, 1994, IDS) was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(b) as being anticipated by Cochran (US Patent 5,047,237) was withdrawn in light of Applicant's amendment.

New Matter

Claims 1-7, 11-16, 20-23, 25, 29, 31-33, 35-36, 38-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This is a new ground of rejection necessitated by Applicants' amendment.***

Amended claims 1, 15, 21, 23, 25 and their dependent claims recite the negative limitation **"wherein said nucleic acid construct is not in the form of a recombinant virus"**. There is literally **no written support** for the specific exclusion of this embodiment in the originally filed specification. While Applicants point out that the sentence on page 5, lines 1-2, of the originally filed specification provides a support for such an amendment. However, the cited sentence states "The nucleic acid construct may be present in a vector construct, for example in a plasmid vector or **in a recombinant viral vector**". It should be noted that a recombinant viral vector is not

necessarily limited to a recombinant virus, for example a recombinant viral vector in the form of a plasmid vector. Thus, it is apparently clear that the cited sentence does not provide support for the specific negative limitation in the amended claims.

Therefore, given the lack of written support provided by the originally filed specification, it would appear that Applicant did not contemplate of the claimed invention at the time the application was filed.

Written Description

Amended claims 1-7, 11-13, 15-16, 20-21, 23, 25, 29, 31-33, 35-36 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons already set forth in the Office action mailed on 4/19/05 (pages 3-6).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. "Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to a method of obtaining expression of an antigen of interest in a mammalian subject, said method comprises transferring into cells of said subject a nucleic acid construct comprising a minimal promoter sequence operably linked to a coding sequence for the antigen, wherein said antigen is expressed in said mammalian cells in an amount sufficient to elicit an immune response to the antigen; a purified and isolated minimal promoter sequence; a vaccine composition comprising the same nucleic acid construct; coated particles suitable for use in particle-mediated nucleic acid immunization, which particles comprise carrier particles coated with the same nucleic acid construct; and a particle acceleration device loaded with the same coated particles. The instant claims encompass compositions and methods of uses involving any minimal promoter sequence, and with respect to claims 13, 21 and 40 any functional variant of a minimal sCMV immediate early promoter sequence or any functional variant of a minimal PRV early promoter sequence.

Apart from disclosing the preparation of 3 human CMV (hCMV), simian CMV (sCMV) and pseudorabies virus (PRV) promoters represented by *Sal1/Bam1*, *Sal1/Sca1* and *Sal1/Not1* fragments of their respective enhanced promoters, the instant specification fails to describe and to provide a representative number of species for a broad genus of minimal promoter that has the same or similar functional properties as those described by the minimal hCMV, sCMV and PRV promoters (e.g., to express the coding sequence of an antigen in an amount sufficient to elicit an immune response to the antigen; particularly a dramatically increased antibody production relative to the enhanced promoters *in vivo*). The instant specification fails to teach which essential or

critical elements that other minimal promoters or other functional variant of a minimal sCMV immediate early promoter or other functional variant of a minimal PRV early promoter need to possess in order to have the same functional properties as those of disclosed minimal hCMV, sCMV and PRV promoters. For example, what are the structural features and/or structural boundaries constituting a minimal promoter for human I-actin promoter, HSP70 promoter, human proliferating cell antigen (PCNA) promoter, and that these minimal promoters would have the same functional properties as those of minimal hCMV, sCMV and PRV promoters? And what are the structural features and/or structural boundaries constituting other functional variants for minimal sCMV and PRV promoters? The prior art at the effective filing date of the present application does not provide description for such a broad genus of a minimal promoter contemplated by Applicant as evidenced by the teachings of Cochran (US Patent 5,047,237), Johnston et al. (U.S. Patent No. 6,194,389; IDS, AK-1), Fischer (U.S. Patent No. 6,156,567), Bujard et al. (U.S. Patent No. 5,888,981) and numerous other references cited below.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48

USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a representative species for a broad genus of a minimal promoter apart from the disclosed minimal hCMV, sCMV and PRV promoters to be utilized in the compositions and methods of uses as claimed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Arguments

Applicant's arguments related in part to the above rejection in the Amendment filed on 10/14/05 (page 8) have been fully considered, but they are respectfully not found persuasive.

Applicant argues that the term "minimal" has been deleted in the amended claims, and a person of ordinary skill in the art would know whether a given sequence was a promoter sequence or an enhancer sequence. Therefore, the specification complies with the Written Description requirement of 35 USC 112, first paragraph.

The amended claims recite "a promoter sequence which is not coupled to its native enhancer sequence". This is a definition of a minimal promoter defined by the instant specification (page 10, lines 10-13); and therefore the above issues remain the same. For example, what are the structural features and/or structural boundaries constituting a promoter sequence which is not coupled with its native enhancer sequence for human I-actin promoter, HSP70 promoter, human proliferating cell antigen (PCNA) promoter, and that these minimal promoters would have the same functional properties as those of disclosed minimal hCMV, sCMV and PRV promoters? Additionally, what are the structural features and/or structural boundaries constituting other functional variants for sCMV and PRV promoters as claimed? Which nucleotides to be deleted, substituted or inserted at which position(s) for these functional variants of sCMV and PRV promoters that do not have their enhancer sequences? The rejection was based mainly on the failure of the instant specification to teach which essential or critical elements that constitute a broad genus of a promoter sequence as broadly claimed.

Furthermore, please note that adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Accordingly, amended claims 1-7, 11-13, 15-16, 20-21, 23, 25, 29, 31-33, 35-36 and 38-40 are still rejected under 35 U.S.C. 112, first paragraph, for the lack of Written Description.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. ***This is a new ground of rejection necessitated by Applicants' amendment.***

The claim is dependent on cancelled claim 8. Accordingly, the metes and bounds of the claim are not clearly determined because it is unclear what exactly do Applicant intend to claim.

Claim Rejections - 35 USC § 102

Claims 1-3, 5-7, 12-14, 25 and 38-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Bujard et al. (U.S. Patent No. 5,888,981) for the same reasons already set forth in the Office action mailed on 4/19/05 (pages 15-16).

Bujard et al. disclose both *in vivo* and *ex vivo* methods for a regulated expression of a gene of interest in a cell in a subject, including human, using a tetracycline-controlled expression system (see abstract and cols. 27-33). The regulated expression system comprises a polynucleotide molecule encoding for a protein of interest, wherein

the polynucleotide is operably linked to a tTA-responsive promoter that contains a minimal hCMV promoter (positions +75 to –53, +75 to –31), and the protein of interest includes the X-protein of HBV (col. 23, lines 22-61), trans-dominant negative tat, rev and env mutants for HIV or transdominant ICp4 mutants for HSV (col. 28, lines 57-67), a viral protein such as adenovirus E19 protein (col. 32, lines 52-55). The expression of such proteins of interest in a subject in the absence of tetracycline would elicit an immune response to the proteins. Bujard et al. also teach the preparation of the minimal promoters hCMV-1* and hCMV*-2 (see col. 36, lines 44-60). Furthermore, the minimal promoters hCMV-1* and hCMV*-2 are functional variants of hCMV immediate early minimal promoter or of the sequence spanning positions 0 to –118 of the hCMV immediate early minimal promoter. It is noted that a functional variant sequence may vary from a native promoter sequence by one or more base substitutions, deletions or insertions as taught by the instant application (see page 10, lines 27-28).

With respect to claims drawn to a vaccine composition, please note that for a composition claim its intended use is not given any patentable weight, particularly the nucleic acid constructs taught by Bujard et al are not distinguishable from the nucleic acid constructs in the vaccine composition of the present invention.

Accordingly, the teachings of Bujard et al. meet the limitation of the instant claims, and therefore Bujard et al. anticipates the instant claims.

Response to Arguments

Applicant's arguments related in part to the above rejection in the Amendment filed on 10/14/05 (pages 9-10) have been fully considered, but they are respectfully not found persuasive.

Applicant argues mainly that the minimal promoters disclosed in Bujard are "virtually silent" by referring to col. 39, lines 42-43, and therefore the constructs of Bujard can not be said to be expression which is sufficient to elicit an immune response to an antigen. Applicants further argue that Bujard does not disclose or suggest eliciting an immune response against a viral, bacterial, parasite or fungal pathogen.

Firstly, it is noted that col. 39, lines 42-43 refer to the "virtual silent" of the minimal promoters hCMV-1* and hCMV*-2 only in the absence of tTA which is inactivated by the presence of tetracycline. As defined by Bujard, a minimal promoter is a partial promoter sequence which defines the transcription start site but which by itself is not capable of, if at all, of initiating transcription **efficiently**. The activity of such minimal promoters depend on the binding of activators such as tetracycline-controlled transactivator to operably linked binding sites (col. 8, lines 36-41). It should be noted that a minimal promoter of the present invention encompasses a promoter containing a heterologous enhancer (see instant specification page 10, lines 10-13), and therefore, the minimal promoters hCMV-1* and hCMV*-2 taught by Bujard meet the limitation of the instant claims.

Secondly, the protein of interest includes the X-protein of HBV (col. 23, lines 22-61), trans-dominant negative tat, rev and env mutants for HIV or transdominant ICp4

mutants for HSV (col. 28, lines 57-67), a viral protein such as adenovirus E19 protein (col. 32, lines 52-55) fall within the scope the recited antigen.

Accordingly, claims 1-3, 5-7, 12-14, 25 and 38-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Bujard et al. (U.S. Patent No. 5,888,981) for the reasons already set forth above.

Claims 1-3, 7, 12-14, 25 and 38-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Fischer (U.S. Patent No. 6,156,567). ***This is a modified rejection necessitated by Applicant's amendment.***

Fischer discloses a recombinant canine adenovirus (CAV) or vector containing a truncated transcriptionally active cytomegalovirus immediate early promoter (e.g., a 91 base pairs in length of human CMV-IE as shown in Figure 20; a 145 base pairs in length of human CMV-IE as set forth in Figure 13C; or a 466 base pairs in length of murine CMV-IE) operably linked to an exogenous DNA, wherein the DNA encodes an antigen of a human pathogen such as a Hepatitis virus antigen (e.g., HbsAg) or HIV antigen such as gp120, gp160 and others (col. 8, line 60 continues to line 51 of col. 10; col. 13, line 5 continues to line 62), as well as an immunogenic or vaccine composition containing the same (col. 11, lines 7-21). Fischer further teaches a method of inducing an immunological response in a host vertebrate, including humans, comprising administering to the host the same immunogenic or vaccine composition (col. 11, line 22 continues to line 44) by parenteral, subcutaneous, intradermal, intramuscular or intravenous injection (col. 30, lines 33-42). Fischer discloses that the compositions can

be administered in dosages and by techniques well known to thoes skilled in the medical arts (col. 30, lines 19-20). Fischer teaches specifically that a truncated promoter can be as little as 10% of the original base pairs of the full-length promoter (col. 13, lines 37-39; col. 15, line 31 continues to line 45 of col. 16). Fischer also teaches that while the promoter and expression cassette are specifically exemplified with reference to adenoviruses, the skilled artisan can adapt these embodiments of the invention to other viruses and to plasmids for cells, such as eukaryotic cells, without undue experimentation, with particular reference to the use of plasmid DNA (col. 33, lines 8-27). Fischer states that "It is therefore within the scope of this invention that the inventive promoter and expression cassette be used in systems other than adenovirus; for example, in plasmids for the direct injection of plasmid DNA" (col. 33, lines 23-27).

With respect to claims drawn to a vaccine composition, please note that for a composition claim its intended use is not given any patentable weight, particularly the recombinant canine adenovirus or vector taught by Fischer is not distinguishable from the nucleic acid construct in the vaccine composition of the present invention.

Accordingly, the teachings of Fischer meet all limitation of the instant claims, and thus the reference anticipates the instant claims as written.

Response to Arguments

Applicant's argument related in part to the above rejection in the Amendment filed on 10/14/05 (page 11) has been fully considered, but it is respectfully not found persuasive.

Applicants argues basically that the amended claims now recite that the claimed construct is not in the form of a recombinant virus, and therefore the claimed invention is not anticipated by Fischer.

Please note that Fischer teaches specifically that while the promoter and expression cassette are specifically exemplified with reference to adenoviruses, the skilled artisan can adapt these embodiments of the invention to other viruses and to plasmids for cells, such as eukaryotic cells, without undue experimentation, with particular reference to the use of plasmid DNA (col. 33, lines 8-27). Please also note that the amended claims do not exclude a recombinant viral vector which is not in the form of a recombinant virus. Fischer teaches compositions, methods of making and using a CAV-based vector that is not a virus.

Claim Rejections - 35 USC § 103

Claims 1-4, 11, 15-16, 20-23, 29, 31-33 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer (U.S. Patent No. 6,156,567) in view of Johnston et al. (U.S. Patent No. 6,194,389; IDS, AK-1). ***This is a new ground of rejection necessitated by Applicant's amendment.***

Fischer discloses a recombinant canine adenovirus (CAV) or vector containing a truncated transcriptionally active cytomegalovirus immediate early promoter (e.g., a 91 base pairs in length of human CMV-IE as shown in Figure 20; a 145 base pairs in length of human CMV-IE as set forth in Figure 13C; or a 466 base pairs in length of murine CMV-IE) operably linked to an exogenous DNA, wherein the DNA encodes an antigen of a human pathogen such as a Hepatitis virus antigen (e.g., HbsAg) or HIV antigen such as gp120, gp160 and others (col. 8, line 60 continues to line 51 of col. 10; col. 13, line 5 continues to line 62), as well as an immunogenic or vaccine composition containing the same (col. 11, lines 7-21). Fischer further teaches a method of inducing an immunological response in a host vertebrate, including humans, comprising administering to the host the same immunogenic or vaccine composition (col. 11, line 22 continues to line 44) by parenteral, subcutaneous, intradermal, intramuscular or intravenous injection (col. 30, lines 33-42). Fischer discloses that the compositions can be administered in dosages and by techniques well known to shoes skilled in the medical arts (col. 30, lines 19-20). Fischer teaches specifically that a truncated promoter can be as little as 10% of the original base pairs of the full-length promoter (col. 13, lines 37-39; col. 15, line 31 continues to line 45 of col. 16). Fischer also teaches that while the promoter and expression cassette are specifically exemplified with reference to adenoviruses, the skilled artisan can adapt these embodiments of the invention to other viruses and to plasmids for cells, such as eukaryotic cells, without undue experimentation, with particular reference to the use of plasmid DNA (col. 33, lines 8-27). Fischer states specifically that "It is therefore within the scope of this

invention that the inventive promoter and expression cassette be used in systems other than adenovirus; for example, in plasmids for the direct injection of plasmid DNA" (col. 33, lines 23-27).

Fischer do not teach specifically that his disclosed compositions to be coated onto carrier particles, a particle acceleration device suitable for particle-mediated nucleic acid immunization being loaded with the same coated particles or a method for expression an antigen of a viral, bacterial, parasite or fungal pathogen via a needleless injection, even though he teaches specifically that his inventive promoter and expression cassette be used in systems other than adenovirus, for example plasmid DNA and the compositions can be administered in dosages and by techniques well known to those skilled in the medical arts.

At the filing date of the present application, Johnston et al. already disclosed a method for obtaining a protective immune response in a vertebrate subject by *in situ* microprojectile bombardment by providing microprojectiles carrying a DNA sequence comprising in the 5' to 3' direction a regulatory element functional in the tissue cells and a gene positioned downstream of the regulatory element and under the transcriptional control thereof, the gene coding for a protective immune response-producing protein or polypeptide, wherein the microprojectiles comprise a material selected from the group consisting of metal (gold, tungsten, iridium), glass, silica, ice, polyethylene, polycarbonate, graphite and diamond; then accelerating the microprojectiles at the subject using a microprojectile acceleration cell transformation apparatus (See abstract, the claims and particularly col. 5 and 6). The polynucleic acid sequence carried by the

microprojectile is a recombinant construct of a gene and a regulatory element, which can be in the form of a plasmid (col. 4, lines 37-51). Exemplary genes that code for proteins or peptides that produce an immune response are genes encoding for subunit vaccines against enteroviruses, surface antigen of the hepatitis B (col. 5, lines 4-14). Johnston et al further teach that the particle bombardment method is surprisingly free of callus formation, inflammation, and other defensive responses, and thus proteins and peptides released from the transformed cells can circulate throughout the treated subject in which the cells reside, and cells which circulate in the subject have accessed to transformed cells (col. 2, line 2 continues to line 5 of col. 3). Additionally, Johnston et al note that an advantage of administering a protein or peptide capable of producing an immune response in this manner is the ability to cause the immunogen to be effectively presented to the subject over an extended period of time, and this is in contrast to the simple injection of protein or peptide, which tend to be rapidly digested and cleared by the subject (col. 5, lines 14-21).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to modify the method of Fischer by adapting the *in situ* microprojectile bombardment approach of Johnston et al to inducing an immunological response in a host vertebrate, including humans against an antigen of a human pathogen such as a Hepatitis virus antigen (e.g., HbsAg) or HIV antigen such as gp120, gp160 and others.

An ordinary skilled artisan would have been motivated to carry out the above modifications because Johnston et al already taught that the particle bombardment method is surprisingly free of callus formation, inflammation, and other defensive

responses, and thus proteins and peptides released from the transformed cells can circulate throughout the treated subject in which the cells reside, and cells which circulate in the subject have accessed to transformed cells (col. 2, line 2 continues to line 5 of col. 3). Additionally, Johnston et al noted that an advantage of administering a protein or peptide capable of producing an immune response in this manner is the ability to cause the immunogen to be effectively presented to the subject over an extended period of time, and therefore would have a more effective immune response.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Fischer and Johnston et al., coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusions

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary, Celine Qian, Ph.D., may be reached at (571) 272-0777, or SPE, Dave Nguyen, at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Quang Nguyen, Ph.D.

CELIAN QIAN
PATENT EXAMINER